Physicians can routinely expect to care for patients from ethnic groups differing from their own. By acknowledging our patients' cultural beliefs, learning more about them, and—when possible—incorporating them into our practice, we will be better prepared to serve this increasingly diverse population.

REFERENCES

1. Barker JC. Cultural diversity—changing the context of medical practice. West J Med 1992; 157:248–254

2. California Department of Finance, Demographic Research Unit. Population Projections by Race/Ethnicity for California and its Counties, 1990–2040. Sacramento, California, 1993

3. Pachter LM. Culture and clinical care: folk illness beliefs and behaviors and their implications for health care delivery. JAMA 1994; 271:690–694

4. Davidson JR. The shadow of life: psychological explanations for placenta rituals. Cult Med Psychy 1985; 9:75–92

5. Fadiman A. The spirit catches you and you fall down: a Hmong child, her American doctors, and the collision of two cultures. New York, NY: Farrar, Straus and Giroux, 1997, p 5

6. Jones E, Kay M. The cultural anthropology of the placenta. *In* Lavery JP (Ed): The Human Placenta. Rockville, MD: Aspen Publishers, 1987, pp 11–23

Zygomycotic Gangrenous Cellulitis in a Patient with Non–Insulin Dependent Diabetes Mellitus

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ZYGOMYCOSIS IS A relatively uncommon fungal infection. Most cases have been reported in association either with diabetes mellitus—usually when complicated by ketoacidosis—or in an immunocompromised host.[1,2] Cutaneous zygomycosis may also complicate extensive soft tissue injuries that occur in a patient without an underlying medical condition.[3,4] We describe a case of cutaneous zygomycosis following minor trauma in a patient with no underlying medical condition except for well-controlled non–insulin dependent diabetes mellitus.

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Report of a Case

The patient, a 78-year-old man, presented with a small, blue-black bulla evolving from an erythematous nodule above the right knee. The lesion had developed over the previous six days following a shallow prick from a splinter of wood. Treatment was started with oral cephalexin (0.5 grams 4 times a day). The patient's medical history included diabetes mellitus for the last seven years. His diabetes was being treated with glibenclamide, and he had postprandial glucose values lower than 190 mg per dl.

A Gram stain of the aspirated bulla revealed a few neutrophils and scarce Gram-positive cocci in clusters; the culture was sterile. Over the subsequent four days, the patient became febrile and a minimally painful necrotic lesion developed over his right knee.

We admitted the patient to the hospital. On physical examination his temperature was 38.3°C (101°F); pulse, 90 beats per minute; and blood pressure, 150/80 mm of mercury. A superficial black necrotic lesion was noted above the right knee, the diameter of which was 10 mm. The knee itself was intact. Distal pulses were palpable. The remainder of the physical examination was unremarkable.

Results of a chest x-ray were normal. Pertinent serum laboratory results were as follows: hemoglobin, 124 grams per liter (12.4 grams per dl); leukocyte count, 10.0×10^9 (10,000 per mm^3) with 80% polymorphonuclears and 7% bands; serum glucose, 9.7 mmol per liter (175 mg per dl); and glycosylated hemoglobin, 8.4% (normal, up to 7%). Renal function tests and electrolyte counts were normal. The serum albumin level was 38 grams per liter (3.8 grams per dl), and serum immunoglobulins were in the normal range. Muscle and liver enzymes were also within the normal ranges.

Intravenous cefazolin (1 gram four times a day) and clindamycin (600 mg three times a day) were begun. In the following three days, the patient remained febrile and the lesion extended proximally. A culture from the wound grew *Enterobacter cloacae*, at which time a regimen of 400 mg of ciprofloxacin intraveneously two times a day and 500 mg of metronidazole four times a day were begun. Two days later, the patient appeared toxic: his temperature was 39.4°C (102.9°F), his pulse was 120 beats per minute, and the necrotic lesion extended further and deeper, involving the patella. Serum laboratory tests revealed a leukocyte count of 16.0×10^9 (16,000 per mm^3) with 85% polymorphonuclears and 10% bands. A swabbed culture of the wound grew *Pseudomonas aeruginosa* and *Enterobacter cloacae*.

A diagnosis of necrotizing fasciitis was made, and extensive débridement of the knee was done, which included a tissue biopsy. The pathologic specimen (Figure 1) revealed broad nonseptate hyphae characteristic of zygomycosis. A culture of the necrotic tissue grew no fungi.

Three drugs were administered: amphotericin B, intraveneously, 50 mg four times a day; ceftazidime, 1 gram three times a day; and amikacin, 500 mg twice a

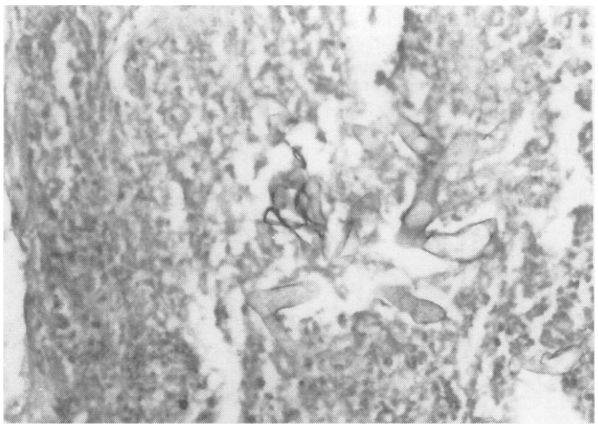

Figure 1.—The figure shows zygomycosis. Note the broad nonseptate, irregularly branching hyphae surrounded by necrotic debris. (PAS×400)

day. There was no improvement in the patient's general condition in the following 48 hours, and signs of necrosis appeared in the perimeter of the débrided area. An amputation above the knee was subsequently undertaken. After the operation, the patient was still febrile and developed adult respiratory distress syndrome, at which time he required intubation and mechanical ventilation.

Wound cultures taken at the time of amputation yielded *Klebsiella pneumoniae* as well as the previously mentioned isolates. The dosages of ceftazidime and amikacin were disconinued, and imipenem cilastatin (1 gram four times a day) was begun. The patient's fever gradually resolved, and, after 14 days, he was weaned from technical ventilation and extubated. Amphotericin B was given in a cumulative dose of 0.5 grams, and six weeks later the patient was discharged. The results of blood cultures taken throughout the course of the illness were all sterile.

The patient was treated with insulin while septic, and glucose values did not exceed 13.88 mmol per liter (250 mg per dl). There was no evidence of ketoacidosis throughout the course of the patient's illness.

Discussion

The incidence of zygomycosis has increased in the last two decades.[5] The patient whose case is presented here experienced primary cutaneous zygomycosis evolving from an ulcer superficial to gangrenous cellulitis; his condition was complicated by secondary bacterial infection and sepsis.

Zygomycete fungi have relatively low pathogenicity; most cases are seen in immunocompromised hosts. There are several risk factors for zygomycosis: diabetes mellitus, especially when complicated by ketoacidosis; immunosuppression, which appears in such patients as those with leukemia, lymphoma, and solid organ and bone marrow transplantation; chronic renal failure; therapy with corticosteroids and deferoxamine; and malnutrition.[1,2]

There are several anatomical classifications of zygomycosis: rhinocerebral, pulmonary cutaneous, gastrointestinal, and widely disseminated.[1,2] In a recent series, cutaneous infection was noted to be prominent.[4] Cutaneous zygomycosis is less often associated with systemic illnesses than are other forms of zygomycosis;[4] it may be acquired by traumatic implantation or through iatrogenic inoculation of the skin with fungi. Cutaneous zygomycosis can be associated with ischemic ulcers in people with diabetes[3,6]; an iatrogenic response following a needle stick in an immunocompromised host[3,4,7]; tissue injury following a trauma or a surgical procedure[3,4]; a wound infection from contaminated elasticized tape[3,8]; or burn-wound infections.[3,9] It is likely that the patient whose case is reported here presented initially with primary zygomycosis after a minor injury from wood splinters.

Hemorrhagic bullas and black necrotic ulcers are typical (but nonspecific) lesions that may occur with cutaneous zygomycosis.[9] The first bacterial wound culture taken from this patient was sterile, and when bacterial infection subsequently developed, appropriate antibiotic therapy was ineffective, which is consistent with primary zygomycosis.

The case we presented is unusual because most patients with well-controlled diabetes, as well as patients who do not have diabetes, have a major systemic predisposing condition or a local injury creating devitalized tissue.[3,4] Patients with well-controlled diabetes and no previous significant injury who *do* experience a case like this usually have infection in the distal extremities, where ischemia because of vascular insufficiency is likely.[10] This patient had no evidence for an underlying immunodeficiency and had well-controlled non–insulin dependent diabetes. The lesion, however, developed after trivial trauma.

All forms of zygomycosis, including cutaneous, are diagnosed by direct microscopic examination of clinical specimens—the ideal specimen being one that was surgically removed. The fungi appear typically as broad, pleomorphic, nonseptate hyphae that branch at a right angle. An examination of lesion scrapings in a potassium hydroxide preparation or with calcofluor white stain may allow for more rapid diagnoses.[1,2] To make species-level identifications, a culture of the fungus from the biopsied tissue and microscopic identification of morphologic features are needed. A culture obtained from a swabbed specimen may yield no fungal growth,[1,2] which is what happened in the case presented here—examining necrotic material that was obtained at surgery led to the diagnosis of cutaneous zygomycosis.

The fungal invasion of vessel walls with subsequent infarction may lead to a vicious cycle in which devitalized tissue enables further fungal and bacterial growth. Bacterial infection may complicate mucormycotic gangrenous cellulitis; the possibility of zygomycosis thus should be considered even if bacteria have been isolated. This is especially true in a predisposed host in whom appropriate antibiotic therapy is ineffective.[11] Zygomycotic gangrenous cellulitis closely resembles necrotizing fasciitis and synergistic cellulitis; clinical criteria alone are unreliable for their differentiation.[10]

Thus surgical excision that includes a biopsy should be performed in all patients who have invasive soft tissue infection that is not readily being controlled by antibiotic therapy alone.[10,12]

The hallmarks of successful treatment for all forms of zygomycosis are early diagnosis, aggressive surgical débridement, systemic antifungal therapy, and control of any underlying disease. Invasive zygomycosis may be cured by extensive débridement—sometimes in the form of amputation—and the intravenous administration of amphotericin B.[4,5] Amphotericin B lipid complex has been used successfully in treating zygomycosis. Lipid formulations of amphotericin B should be considered for patients with zygomycosis and severe renal impairment because of the nephrotoxicity of the conventional form of amphotericin B and the chance of systemic zygomycosis affecting the kidneys.[13] Both the optimal duration and the total amount of intravenous amphotericin B for zygomycosis are unknown; they should be individualized according to the patient's clinical response.

Azole antifungals have been found to be completely ineffective in comparison to amphotericin B in an animal model of zygomycosis.[14] There are few reported successful outcomes of zygomycosis with fluconazole therapy.[15] The relative contribution of fluconazole administration beyond surgical débridement and reversion of the underlying immunosuppression cannot be determined in these cases.

The prognosis of the cutaneous form of zygomycosis is better than its other forms, which is probably due to the enhanced feasibility of surgical débridement.[4] As this case demonstrates, invasive zygomycosis can follow mild injury in patients without classic predisposing factors. Zygomycosis should be considered in the differential diagnosis of progressive necrotizing skin infection. It is important to note that isolating bacteria does not exclude zygomycosis.

REFERENCES

1. Lehrer RI, Howard DH, Sypherd PS, Edwards JE, Segai GP, Winston DJ. Zygomycosis—UCLA Conference. Ann Intern Med 1980; 93:93–108

2. Rinaldi MG. Zygomycosis. Infect Dis Clin North Am 1989; 3:19–41

3. Johnson PC, Satterwhite TK, Monheit JE, Parks D. Primary cutaneous zygomycosis in trauma patients. J Trauma 1987; 27:437–441

4. Adam RD, Hunter G, DiTomasso J, Comerci G. Zygomycosis: Emerging prominence of cutaneous infections. Clin Infect Dis 1994; 19:67–69

5. Parfrey NA. Improved diagnosis and prognosis of zygomycosis—a clinicopathologic study of 33 cases. Medicine 1986; 65:113–123

6. Tomford JW, Whittley D, Ellner JJ, Tomaschefski JF. Invasive primary cutaneous phycomycosis in diabetic leg ulcers. Arch Surg 1980; 115:770–771

7. Veliath AJ, Rao R, Prabhu MR, Aurora AL. Cutaneous phycomycosis (zygomycosis)with fatal pulmonary dissemination. Arch Dermatol 1976; 112:509–512

8. Gartenberg G, Bottone EJ, Keusch GT, Weitzman I. Hospital acquired zygomycosis (Rhizopus rhizopodiformis) of skin and subcutaneous tissue: epidemiology, mycology and treatment. N Engl J Med 1978; 299:1115–1118

9. Nash G, Foley FD, Goodwin MN Jr, Bruck HM, Greenwald KA, Pruit BA Jr. Fungal burn wound infection. JAMA 1971; 215:1664–1666

10. Wilson CB, Siber GR, O'Brien TF, Morgan AP. Phycomycotic gangrenous cellulitis. Arch Surg 1976; 111:532–538

11. Vainrub B, Macareno A, Mandel S, Musher DM. Wound zygomycosis (mucormycosis) in otherwise healthy adults. Am J Med 1988; 84 546–548

12. Rouse TM, Malangoni MA, Schulte WJ. Necrotizing fascitis: a preventable disaster. Surgery 1982; 92:765–770

13. Gonzalez CE, Couriel DR, Walsh TJ. Disseminated zygomycosisin aneutropenic patient: successful treatment with amphotericin B lipid complex and granulocyte colony-stimulating factor. Clin Infect Dis 1997; 24:192–196

14. Van Cutsem J, Van Garven F, Fransen J, Jansssen PAJ. Treatment of experimental zygomycosis in guinea pig with azoles and with amphotericin B. Chemotherapy 1989; 35:267–272

15. Kocak R, Tetiker T, Kocak M, Baslamisli F, Zorludemir S, Gonlusen G. Fluconazole in the treatment of three cases of Zygomycosis. Eur J Clin Microbiol Infect Dis 1995; 14:559–561 (Letter)

Administration of a Neuromuscular Blocking Agent and a Narcotic Agent Mimicking Posterior Urethral Valves

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URINARY RETENTION in male neonates demands evaluation for the presence of posterior urethral valves. Urinary retention can be iatrogenic, however, if ill neonates are heavily medicated in the absence of a urethral catheter.

Report of a Case

A male infant was delivered to a healthy 26-year-old gravida 4, para 0 (G_4P_0) woman at 34 weeks gestation through a spontaneous vaginal delivery. The child was noted to have normal external genitalia and normal voiding, with a serum creatinine level of 0.8 mg per dl. At 2 days of age, he developed respiratory distress and required intubation; pancuronium and fentanyl were employed for paralysis and sedation. No urethral catheter was placed. One week later, he developed anuria and had a serum creatinine level of 3.0 mg per dl. A physical examination revealed normal external genitalia and suprapubic fullness. Results of ultrasonography showed a distended bladder and bilateral hydronephrosis, consistent with the presence of posterior urethral valves. The renal parenchyma, however, appeared to be of normal echogenicity and thickness for the infant's age (Figure 1).

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